NANOTUBE COATINGS FOR IMPLANTABLE ELECTRODES

CROSS-REFERENCE TO RELATED APPLICATION

The present application claims priority from U.S. provisional application Serial No. 60/429,471, filed November 26, 2002.

BACKGROUND OF THE INVENTION

1.   Field of the Invention

This invention generally relates to coatings for implantable electrodes such as pacing electrodes, neurostimulator electrodes, and electroporating electrodes and sensing electrodes. The three overriding requirements for these types of electrodes are biocompatibility, biostability, and low energy loss. Broadly, the biocompatibility requirement is met if contact of the electrode with body tissue and blood results in little or no immune response from the body, especially thrombogenicity (clotting) and encapsulation of the electrode with fibrotic tissue. The biostability requirement means that all physical, electrical, and chemical properties of the electrode/coating system remain constant and unchanged over the life of the patient. The low energy loss requirement is met if electrode polarization is a minimum.

2.   Prior Art

U.S. Patent No. 4,602,637 to Elmqvist describes a commonly used pacing electrode having sputtered columnar titanium nitride as a coating material. This form of titanium nitride has good conductivity combined with a high specific surface area, resulting in favorable polarization and sensing properties. The disadvantage of titanium nitride, however, is that it degrades the electrical properties of surrounding tissue after implantation. This occurs as the body tissue encapsulates the columnar titanium nitride in fibrotic tissue, which has a lower conductivity than normal tissue.

In the case of a pacing electrode, fibrotic tissue raises the stimulation threshold. The stimulation threshold is the minimum energy required to produce a cardiac contraction. This, in turn, impacts the battery life of the system so that the medical device must be explanted sooner than desired. The encapsulation process also interferes with sensing of intrinsic milivolt signals required by pacemakers. In prior electrode designs, the fibrotic encapsulation problem has been addressed by incorporating a means of metering or eluting steroidal medication to the site of tissue contact over time. However, eluting a steroidal medication to the implant site is not completely effective in eliminating the stimulation threshold rise due to encapsulation. Steroidal medication eluting arrangements have a short duration of effectiveness, and also add cost and complexity to the system, add the risk of infection, and, in many cases, a portion of the electrode working surface must be dedicated to the medication administering function.

Other efforts to overcome the problem of fibrotic encapsulation are described in U.S. Patent Nos. 4,495,039 to Cerise et al. and 4,612,100 to Edeling et al. The former patent relates to electrodes made of pyrolytic carbon while the latter is directed to electrodes coated with amorphous sputtered carbon. These designs meet the requirement of improved biocompatibility, but they do not have the high specific surface characteristics of columnar titanium nitride, and so fall short in polarization and sensing properties.

SUMMARY OF THE INVENTION

The present coating consists of a substrate surface layer comprised of conductive carbonaceous nanotubes or nanotubes of other biocompatible, conductive material. The nanotubes are in the form of single-wall nanotubes (below about 2 nanometers in diameter), multiwall nanotubes (structure of concentric tubes), nanotube ropes, carbon whiskers, and a combination thereof. Multiwall nanotubes are nanotubes grown concentrically. Nanotube ropes consist of a multitude of single- or multi-walled nanotubes bundled in parallel until the diameter increases, typically to about 10 nm to about 100 nm. Nanotube ropes originate at the substrate and grow outward. They can grow into a parallel, close-packed morphology, or into a tangled "hairy" morphology. In either case, the result is a layer consisting of a multitude of nanotubes, each attached at one or both ends to the substrate. The nanotubes can be carbonaceous, or of other conductive and biocompatible nanotube-forming materials, such as carbon-doped boron nitride.

The resulting electrode is both biocompatible and biostable because the nanotube coating is covalently bonded to the electrode surface. Advantageously, the electrode exhibits relatively low polarization because of the greatly increased surface area imparted by the nanotubes. In that respect, the nanotube coating mimics the physical structure of the conventional sputter coated columnar titanium nitride. However, the excellent biocompatibility of nanotube coatings advantageously lessens or eliminates the requirement for a means of providing steroidal medication to the tissue surrounding the electrode.

These and other aspects of the present invention will become increasingly apparent to those skilled in the art by reference to the following description and to the appended drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a photograph of nanotube ropes grown on a titanium substrate from acetylene at 650°C at 100,000x magnification.

Figs. 2A and 2B are photographs at 50,000 magnification of nanotube whiskers grown on a titanium substrate from methyl acetylene-propadiene gas bubbled through ammonium hydroxide at 550°C and 650°C, respectively.

Figs. 3A and 3B are photographs showing a nanotube coating grown *in-situ* on a tantalum substrate according to one embodiment of the present invention at magnifications of 20,000x and 50,000x, respectively.

Fig. 4 is a photograph at 20,000x magnification showing a layer of nanotubes bonded to a glass surface

using an iridium oxide binder according to another
embodiment of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

One preferred embodiment for making a nanotube-coated
electrode is by high temperature hydrocarbon decomposition
on a substrate. The substrate material must be
biocompatible, electrically conductive, and capable of
nucleating or catalyzing the desired nanotube structures.
Preferred substrate materials include tantalum, titanium,
zirconium, platinum, iridium, and niobium. A different
base material can be used if the substrate is provided with
a coating of these metals or with a coating of a nitride,
carbide, carbonitride, or oxide of these metals. An
example of this is a tantalum coating on a titanium
substrate. Both materials are biocompatible, however,
titanium is less expensive than tantalum.

Carbon is another preferred catalyst material for
growing nanotubes. Preferably, the carbon is in the form
of a machined vitreous carbon electrode or as a thin film
carbonaceous coating over a machined metal electrode.
Sputtering is one preferred method for applying a
relatively thin film carbon coating, in which case the
coating consists of amorphous carbon. In particular, if
the sputtered amorphous carbon is doped with nitrogen, such
as by the presence of nitrogen in the sputter process gas,
then the resulting film is an effective catalyst for
subsequent growth of nanotubes. If nitrogen is provided,
it is preferably at a concentration of about 1 to about 57
atomic percent. The advantage of this carbon
nanotube/carbon catalyst system is that the electrode-

tissue interface is limited to various allotropes of carbon, which are highly biocompatible materials. That is, when the metal substrate is first provided with sputtered amorphous carbon, it is prevented from being exposed to body fluids and body tissue. If the catalyst layer were a biocompatible metal rather than carbon, the porous nanotube layer would allow the metal to be exposed to body fluids and tissue.

U.S. Patent Nos. 5,872,422 and 5,973,444, both to Xu et al., describe a conventional process for growing a carbon fiber on a metallic substrate, such as for use in a picture tube. However, the present invention has adapted this process for the production of a nanotube-coated electrode. The process begins with a shaped electrode substrate made of or coated with the appropriate catalyst material first being placed in a closed chamber with a flowing hydrogen atmosphere. The chamber is heated to a temperature from about 350°C to about 1150°C, more preferably from about 550°C to about 850°C. When the desired temperature is reached, the hydrocarbon flow is started. Hydrocarbons useful for growing nanotubes are gaseous and include acetylene, methyl acetylene-propadiene (MAPP) gas, and a gas from the paraffin series, i.e., methane, ethane, propane, butane, pentane, etc, and mixtures thereof. Additionally, having been bubbled through an ammonium hydroxide solution can provide the hydrocarbon with an ammonia addition. A typical coating formation time is about 5 minutes to about 1 hour, preferably about 15 minutes. Cooling is done in hydrogen. The resulting nanotubes are generally classified as being nanotube ropes.

Plasma assisted chemical vapor deposition is another preferred method for making a nanotube-coated electrode substrate. The plasma assisted CVD process can be performed by microwave excitation, or by other means. This process is preferred because the resulting nanotube arrays are more highly aligned, which is an objective in attempting to mimic a conventional columnar titanium nitride coating.

The morphology of the nanotubes is partially impacted by the hydrogen source gas. For example, acetylene at about 650°C gives nanotube ropes about 20 to 50 nm in diameter (Fig. 1). Changing to MAPP gas bubbled through NH_3OH with a heating temperature of about 550°C results in coarse, more tightly adhering, oriented spiky carbon whiskers (Figs. 2A and 2B).

Alternatively, bulk loose nanotubes are attached to the electrode surface by means of a thin film binder coating consisting of a biocompatible metal or conductive metal oxide deposited by means of a metal compound precursor in liquid form. The basic method of thin film deposition is described in greater detail in U.S. Patent No. 4,919,135 to Phillips, which is incorporated herein by reference. Bulk nanotubes are commercially available from numerous sources; for example: Nanostructured and Amorphous Materials, Inc (Los Alamos,NM). Suitable binder precursors include chloroiridic acid (hydrogen hexachloroiridate IV hydrate), chloroplatinic acid, titanium (IV) chloride, zirconium (IV) chloride, niobium (V) chloride, tantalum (V) chloride, and mixtures thereof. The binder is prepared at room temperature by first dissolving the precursor compound of the biocompatible metal in a solvent. Preferred

solvents are alcohols such as *tert*-butanol, isopropanol, and ethanol.

Loose nanotubes are then mixed into the precursor solution at a high shear rate. The resulting homogeneous mixture is applied to the electrode surface as a thin film by dipping, spraying, doctor blading, by dropper application, or otherwise contacting the metal compound/solvent/nanotube mixture thereto. Solvent removal is by drying the substrate in a warmed atmosphere. This produces a thin metal compound/nanotube layer on the electrode surface. A low temperature heat treatment converts the metal compound layer to a metal/nanotube or metal oxide/nanotube composite thin film. This heating step is carried out at a temperature of about 300°C to about 500°C for a time ranging from about 30 minutes to about 3 hours. The resulting thin film has a thickness of about 100 to 500 nanometers, and resembles a porous metal matrix composite with the biocompatible conductive metal oxide or metal as the matrix and the nanotubes being the second phase.

In the case of an iridium oxide binder formed from chloroiridic acid, iridium metal is easily oxidized, and a metal oxide binder results. The preferred converting atmosphere is air. In the case of a binder of platinum, titanium, zirconium, niobium, and tantalum, the respective platinum, titanium, zirconium, niobium, and tantalum metals do not oxidize at the temperatures used. Instead, heating the precursors of these metals in an inert atmosphere, such as of argon, nitrogen, helium, and a vacuum, is expected to result in a metal binder.

The following examples describe the manner and process of a nanotube-coated substrate according to the present

invention, and set forth the best mode contemplated by the inventors of carrying out the invention.

EXAMPLE I

A tantalum substrate was placed in a closed chamber. The chamber was heated to about 650°C with hydrogen gas flowing through the chamber at a rate of about 1 liter/min. for about every 20 cc of reactive volume. When the reaction chamber reached the desired temperature, 0.5 liter/min of acetylene was added to the reaction gas stream. After about 15 minutes, it was observed that a useable nanotube coating had grown *in-situ* on the tantalum substrate. The photographs in Figs. 3A and 3B show the resulting *in-situ* grown nanotube coating on the tantalum substrate at magnifications of 20,000x and 50,000x, respectively.

A useable nanotube coating can be grown in a similar manner on a substrate of titanium, zirconium, iridium, platinum, niobium, and nitrogen-doped amorphous carbon, or virtually any substrate provided with a thin film coating of these materials. These catalytic or nucleating materials have biocompatible properties similar to those of tantalum.

EXAMPLE II

Etching in aqueous oxalic acid solution at 80°C for 1 hour cleaned a titanium electrode tip.

A chloroiridic acid solution was prepared by dissolving 1 gram of chloroiridic acid in 35 ml of isopropyl alcohol at room temperature with stirring. Loose

nanotube powder was then added while stirring at a high shear rate until a thick, viscous mixture was obtained. The iridium oxide coated substrate was then dipped into the mixture to provide a viscous coating of nanotubes thereon. Heating the coated substrate to about 340°C in air for about 1 hour converted the metal chloride to iridium metal, which was then subsequently oxidized by further heating. The iridium oxide coated substrate had embedded nanotubes.

The photograph in Fig. 4 shows a similarly generated nanotube coating bonded to a PYREX® glass substrate with iridium oxide binder at a magnification of 20,000x. While the experiment was done with a titanium electrode tip, the reason for the glass substrate was because glass is easily fractured and then viewed edge-on in the SEM in order to image a cross section of the thin film coating. With sub-micron coatings it is very difficult to get a cross section from the titanium part itself. PYREX® glass was used because it withstands the 340°C heat treatment without softening or shattering.

It is appreciated that various modifications to the inventive concepts described herein may be apparent to those of ordinary skill in the art without departing from the spirit and scope of the present invention as defined by the appended claims.